or Q41R; (3) a Group 4 amino acid residue mutated to a Group 2 amino acid residue at position 52, for example, the mutation represented by T52I; (4) a Group 4 amino acid residue mutated to a Group 3 amino acid residue at position 52, for example, the mutation represented by T52N; (5) a Group 4 amino acid residue mutated to a Group 5 amino acid residue at position 73, for example, the mutation represented by C73R; (6) a Group 1 amino acid residue mutated to a Group 4 amino acid residue at position 101, for example, the mutation represented by P101S; (7) a Group 1 amino acid residue mutated to a Group 3 amino acid residue at position 101, for example, the mutation represented by P101Q; (8) a valine amino acid residue mutated to another Group 2 amino acid residue at position 111, for example, the mutation represented by V111I; (9) a Group 4 amino acid residue mutated to a Group 2 amino acid residue at position 133, for example, the mutation represented by S133L; (10) a Group 3 amino acid residue mutated to a Group 2 amino acid residue at position 141, for example, the mutation represented by E141V; (11) a Group 3 amino acid residue mutated to a Group 5 amino acid residue at position 141, for example, the mutation represented by E141K; (12) a Group 4 amino acid residue mutated to Group 6 amino acid residue at position 153, for example, the mutation represented by C153Y; (13) a Group 4 amino acid residue mutated to a Group 5 amino acid residue at position 153, for example, the mutation represented by C153R; (14) a Group 4 amino acid residue mutated to a Group 1 amino acid residue at position 281, for example, the mutation represented by T281A; (15) a Group 3 amino acid residue mutated to a Group 2 amino acid residue at position 367, for example, the mutation represented by N367I; (16) a Group 3 amino acid residue mutated to a Group 6 amino acid residue at position 367, for example, the mutation represented by N367Y; (17) a Group 1 amino acid residue mutated to Group 4 amino acid residue at position 389, for example, the mutation represented by P389S; and/or (18) a Group 1 amino acid residue mutated to a Group 2 amino acid residue at

position 389, for example, the mutation represented by P389L.

In certain embodiments of this aspect of the invention, the variant protein of the lovE protein sequence has an amino acid sequence of SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, or SEQ ID NO:65.

In another embodiment thereof, the variant protein of the lovE protein is encoded by a nucleic acid molecule having a polynucleotide sequence of SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:81, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, or SEQ ID NO:90.

In a sixth aspect, the invention provides a fungus having improved lovastatin production made by the process of transforming a fungal cell with a nucleic acid molecule encoding a variant of the lovE protein of the first aspect of the invention. In an embodiment thereof, the nucleic acid molecule is selected from a nucleic acid molecule of the second aspect of the invention.

In a seventh aspect, the invention provides an improved process for making lovastatin comprising transforming a fungal cell with a nucleic acid molecule encoding a variant of the lovE protein of the first aspect of the invention. In an embodiment thereof, the fungal cell is transformed with a nucleic acid molecule of the second aspect of the invention.

International Patent Application PCT/US99/29583 discloses lovastatin production genes. However, this reference does not provide a mature *lovE* cDNA sequence. The invention herein remedies the shortcoming of this

reference by providing a complete cDNA sequence for the *lovE* mRNA.

In an eighth aspect, the invention provides a nucleic acid molecule encoding a lovE protein defined by SEQ ID NO:91. In an embodiment thereof, the invention provides an isolated *lovE* nucleic acid molecule defined by SEQ ID NO:92.

The following examples illustrate the preferred modes of making and practicing the present invention but are not meant to limit the scope of the invention since alternative methods may be utilized to obtain similar results.

EXAMPLES

Example 1: Preparation of Strains and Plasmids

Strain MY2124 was derived from the Sigma 1278b strain background of *S. cerevisiae* and its complete genotype is as follows: *MATα/MATα::LEU2 ura3Δ0 /ura3Δ0 leu2Δ0/leu2Δ0 trp1Δ0::hisG/trp1Δ0::hisG his3Δ0::hisG/his3Δ0::hisG ura3Δ0::lovF-HIS3p-neo/ura3Δ0*. MY2124 can be constructed by mating *S. cerevisiae* strains MY2112 (*MATα ura3Δ0 leu2Δ0 trp1Δ0::hisG his3Δ0::hisG ura3Δ0::lovFp-HIS3p-neo*) with MY1555 (*matα::LEU2 ura3Δ0 leu2Δ0 trp1Δ0::hisG his3Δ0::hisG*) and isolating zygotes. The *ura3Δ0::lovFp-HIS3p-neo* allele of MY2112 was derived by cotransforming *Sfi*I-linearized plasmid MB2254 with pRS424 (Sikorski and Hieter (1989) *Genetics* 122:19-27) into MY1413 (*MATα leu2Δ0 trp1Δ0::hisG his3Δ0::hisG*). Transformants were selected on SC-Trp media and subsequently screened for 5-fluoro-orotic acid resistance to identify those transformants containing the *ura3Δ0::lovFp-HIS3p-neo* allele. Trp$^-$ segregants lacking plasmid pRS424 were isolated by growing the strain under non-selective conditions.